Federal response to COVID-19: Monoclonal Antibody Playbook

Outpatient administration playbook version 2.2

25 FEB 2021
Introduction

Comprehensive checklist overview

Activity 1: Define facilities and patient visit logistics
- Site will need dedicated outpatient COVID-19 treatment space
- Alternate site of care allowances and needs
- Manage patient flow in accordance with CDC guidelines
- Pharmacy Needs
- Testing Needs
- High level guidance on product shipping and storage

Activity 2: Ensure sufficient supplies
- Site supplies needed: Standard infusion supplies are needed but several components have been difficult to source

Activity 3: Develop plan for staffing and personnel
- Treating patients needs support of healthcare providers, pharmacist, and nurses

Activity 4: Review drug administration process
- Multiple treatment pathways for symptomatic COVID-19 patients to receive care

Activity 5: Prepare for reimbursement and drug ordering
- Reimbursement process for mAbs therapeutic under EUA

Activity 6: Reporting process
- Reporting Needs

Product specific supplements to this playbook will also be made available by manufacturers
Introduction
This playbook is intended to support sites interested in administering COVID-19 treatment under EUA including:

- Existing hospital or community-based infusion centers
- Existing clinical space (e.g. urgent care, emergency depts)
- Ad hoc new infusion sites (e.g. "hospitals without walls")
- Long-term care facilities or home infusions with infusion delivery capability

Initial version of playbook focused on:

- Monoclonal antibody treatment
- Delivery via infusion
- Outpatient setting

This playbook will continue to evolve as other treatments and administration methods become available. We hope this playbook will be used to help healthcare facilities to implement monoclonal antibody treatment in an outpatient setting for those with COVID-19.
Context of mAbs outpatient administration playbook

Proven operationally challenging to run monoclonal antibodies clinical trials in outpatient setting for variety of reasons

Recent EUAs have been granted for Eli Lilly and Regeneron only for outpatient setting

Few sites likely to have experience with this type of procedure in an outpatient setting with COVID-19 patients

Scope of this playbook

Goal of playbook to articulate what is needed for outpatient administration to potential Tx sites:

- **Supplies likely required** for administration and potential challenges in procurement
- **Personnel needed** for infusions
- **Space and logistics** needed to safely treat COVID-19 patients and protect others
- **Drug administration** process
- **Reimbursement** process
- **Reporting** process

**Elements currently out of scope**

- Process for site engagement with state health departments on ordering or reporting
- Mechanisms for communication with United States Government on allocation or distribution

To be addressed in future versions of the playbook
Monoclonal antibodies (mAbs) directly neutralize the COVID-19 virus and are intended to prevent progression of disease. mAbs likely to be most effective when given early in infection. Product delivered via single administration (e.g., IV infusion). Early evidence appears to suggest promise of mAb products in outpatient settings:

- Early evidence from Eli Lilly mAb showed potential to reduce hospitalization for infected people if given early in infection in BLAZE-1 clinical trial.
- Early evidence from Regeneron mAb cocktail data showed potential to decrease viral load and reduced medical visits in infected people if given early in the Outpatient 2067 clinical trial.
mAbs products now available under EUA therefore...

Administration site does not need to be a clinical trial site to administer product

Informed consent is not needed to administer products under EUA

No clinical data reporting required beyond established mechanisms for tracking and reporting serious adverse events; teletracking data reporting required on utilization of product
Treatment eligibility

Products granted EUA for mild to moderate COVID-19 cases early in infection, who are at high risk for progressing to severe COVID-19 and/or hospitalization; with following criteria:

- Confirmation via positive PCR or antigen test
- Treatment as soon as possible following positive viral test and within 10 days of symptom onset
- Patient symptomatic but not yet progressed to require hospitalization or oxygen therapy

Treatment recommended just for high-risk adult and pediatric patients 12 years and older >40 kgs – high-risk defined as patients who meet at least one of following criteria:

<table>
<thead>
<tr>
<th>High-risk criteria (adults)</th>
<th>High-risk criteria (pediatric)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ave BMI ≥ 35</td>
<td>12-17 years of age AND have</td>
</tr>
<tr>
<td>Have chronic kidney disease</td>
<td>BMI 85&lt;sup&gt;th&lt;/sup&gt; percentile for age/gender based on CDC growth charts, OR</td>
</tr>
<tr>
<td>Have diabetes</td>
<td>Sickle cell disease, OR</td>
</tr>
<tr>
<td>Have immunosuppressive disease</td>
<td>Congenital or acquired heart disease, OR</td>
</tr>
<tr>
<td>Are currently receiving immunosuppressive treatment</td>
<td>Neurodevelopmental disorders, OR</td>
</tr>
<tr>
<td>Are ≥ 65 years of age</td>
<td>A medical-related technological dependence, OR</td>
</tr>
<tr>
<td>Are 55 years of age AND have</td>
<td>Asthma, reactive airway or other chronic resp. disease that requires daily meds/control</td>
</tr>
<tr>
<td>- Cardiovascular disease, OR</td>
<td>- Chronic obstructive pulmonary disease (or others)</td>
</tr>
<tr>
<td>- Hypertension, OR</td>
<td></td>
</tr>
<tr>
<td>- A medical-related technological dependence, OR</td>
<td></td>
</tr>
<tr>
<td>- Asthma, reactive airway or other chronic resp. disease that requires daily meds/control</td>
<td></td>
</tr>
</tbody>
</table>

Please reference EUA factsheets for specific treatment guidelines and detailed definitions of high-risk patients

For your awareness (e.g. for patients not eligible for treatment under EUA):

Monoclonal antibodies under evaluation for additional indications

Participation encouraged in clinical trials to assess additional drugs and indications

Clinical trial information available at

http://www.riseabovecovid.org

Lilly clinical trials:
https://blaze2study.com/

Regeneron clinical trials:
https://www.regeneron.com/covid19
**EUA summary: Eli Lilly Bamlanivimab**

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

**Bamlanivimab is not authorized for use in patients:**
- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity

**Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19.** Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Bamlanivimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

For additional information—please reference EUA factsheet.

**Key caveats**

The EUA is for the use of the unapproved product bamlanivimab to treat COVID-19.

Bamlanivimab is an investigational drug that has not been approved by the FDA for any use; and should not be considered the standard of care for treatment of patients with COVID-19.

It is not yet known if bamlanivimab is safe and effective for the treatment of COVID-19.

This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use, unless the authorization is terminated or revoked sooner.

Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS related to bamlanivimab.
**EUA summary: Regeneron (casirivimab/imdevimab)**

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products casirivimab/imdevimab to be administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Casirivimab/Imdevimab are not authorized for use in patients:

- who are hospitalized due to COVID-19, or
- who require oxygen therapy due to COVID-19, or
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity

**Benefit of treatment with casirivimab/imdevimab has not been observed in patients hospitalized due to COVID-19.** Monoclonal antibodies, such as casirivimab/imdevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Casirivimab/imdevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

For additional information—please reference EUA factsheet and RegeneronEUA.com

**Key caveats**

The EUA is for the use of the unapproved products casirivimab/imdevimab to treat COVID-19.

Casirivimab/imdevimab are investigational drugs that have not been approved by the FDA for any use; and should not be considered the standard of care for treatment of patients with COVID-19.

It is not yet known if casirivimab/imdevimab are safe and effective for the treatment of COVID-19.

This use is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use, unless the authorization is terminated or revoked sooner.

Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS related to casirivimab/imdevimab.
EUA summary: Eli Lilly (bamlanivimab/etesevimab)

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products bamlanivimab/etesevimab to be administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

Bamlanivimab/etesevimab are not authorized for use in patients:
- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity

Benefit of treatment with bamlanivimab/etesevimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab/etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Bamlanivimab/etesevimab may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

For additional information—please reference EUA factsheet.

Key caveats

The EUA is for the use of the unapproved products bamlanivimab/etesevimab to treat COVID-19.

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Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS related to bamlanivimab/etesevimab.
Based on what we have learned to date - early administration of treatment needs fast testing turnaround and patient scheduling

Planning required for "Test and treat" or "Test and refer" models

Overview
- Treatment likely most beneficial to patients if given early in symptom progression
- EUA requires administration of treatment as soon as possible after confirmed positive test result and within 10 days of symptom onset
- Strong partnership and communication between patients and HCP to get right treatment to right patients at right time
- Fast testing turnaround needed, to efficiently identify positive tests and schedule for treatment

Example of timeline which would fulfill EUA requirements

<table>
<thead>
<tr>
<th>Event</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of symptoms</td>
<td></td>
</tr>
<tr>
<td>Clinical visit and diagnostic test</td>
<td>≤ 3 days post symptom onset</td>
</tr>
<tr>
<td>Confirmed positive test</td>
<td>≤ 2 days post diagnostic test</td>
</tr>
<tr>
<td>Treatment</td>
<td>≤3 days post positive test result</td>
</tr>
</tbody>
</table>

Treatment needed within 10 days of symptom onset

Testing sites should recommend COVID+ patients that are high risk confer with their HCP on potential suitability for Tx

Please reference EUA factsheet for specific treatment guidelines including recommended treatment window
Key challenges to overcome to allow for successful administration of mAb in outpatient setting

Drug ordering and storage

- Pre-treatment
- Treatment
- Post-treatment

Communication on supply

Out of scope of this playbook

For Additional Information
Reference: ASPR's Portfolio of COVID-19 Medical Countermeasures

Key challenges for administration
- Many sites not adequately outfitted to do infusions in outpatient setting (besides hospitals and ERs)
- Existing infusion centers currently treat immune-compromised patients, would need to be clear processes for COVID-19
- Pre-existing infusion centers potentially need to adjust protocols to treat COVID-19-positive patients
- Lengthy infusion process (up to 1 hour infusion followed by 1 hour post-infusion monitoring) needing dedicated space and personnel
- Quick turn-around time for testing needed to diagnose patients within window for treatment

Please reference EUA factsheet for specific treatment guidelines

1. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
Federal response playbook for Healthcare administrators

Objective to summarize requirements to administer monoclonal antibodies for healthcare facilities interested in administering the product

This document

Eli Lilly Infusion Units for COVID-19 Antibody Treatment

Objective to provide recommendations for establishing infusion units to treat COVID-19 patients in diverse settings

Infusion units for COVID-19 Antibody treatment link

Eli Lilly Bamlanivimab Antibody Playbook

Objective to help sites of care operationalize a Bamlanivimab antibody response to COVID-19 across varying infusion sites of care


Regeneron EUA guidebook

Provides additional detail on administration requirements for Regeneron mAbs product

Please note… EUA guidelines continue to evolve

Please reference EUA fact-sheets for latest treatment guidelines and information

FDA continues to update dilution requirements and infusion times based on latest clinical information
Comprehensive checklist overview
Plan of action to administer monoclonal antibodies under outpatient EUA

Confirm your site wants to participate

- Review needs for treatment in outpatient settings
- Ensure site prepared to meet needs for treatment or willing to make required investments
- Confirm site leadership supportive of participation
  - Including senior clinical leadership (e.g., Chief Medical Officer)
- Approval of product for use by the hospital’s Pharmacy and Therapeutics Committee (or equivalent committee)
- Coordinate with State Chief Medical Officers to confirm participation

Prepare your site and staff for outpatient mAbs administration

- Ensure sufficient supply of needed materials for treatment
  - Infusion supplies, resuscitation equipment, etc.
- Develop staffing and personnel plan to support treatment
- Allocate needed facilities and equipment to support administration
- Ensure existing infection prevention plan sufficient
  - Adjust existing plan if needed to safely manage patient flow
  - Consider potential security requirements if needed
- Review drug administration needs with staff
- Inquire with hospital leadership about reimbursement process
- Prepare for adverse events data tracking process

Develop procedures to identify and treat patients in timely manner

- Prepare for scheduling and routing of referrals from testing center or other HCPs to treatment
- Ensure hospital staff and doctors are aware of outpatient treatment availability
- Ensure patient privacy (HIPAA compliant) maintained during process
- Communicate to patient that EUA issued for investigational treatment but does not constitute research on behalf of the hospital
Readiness checklist: Administration of outpatient mAbs under EUA

Allocate **dedicated space** and develop plan to **manage patient flow**
- Clear process for patients that are coming to clinical site including scheduling requirements
- Admission process for COVID-19 positive patients designed to minimize risk of spread per facility requirements / directions / guidelines'
- Dedicated room available for treatment

Ensure **dedicated source of supplies**; which may be difficult to procure
- Needed infusion components obtained
  - Example: IV kits, infusion chair, IV pole, vital sign monitoring equipment, emergency medications

Assign **sufficient personnel** to meet expected demand
- Sufficient staffing plans in place for Nurse/IV tech, Physician, Pharmacist or other licensed medical professional
  - Likely need dedicated team to treat patients

Prepare for **drug administration** process
- Pre–visit: Clear treatment and monitoring plan developed for during infusion
- Treatment: 1-hour treatment\(^2\) and 1-hour post-treatment observation
  - Emergency protocol defined for addressing potential infusion reactions or complications
- Post-treatment: Clear process for patient follow-up defined using telemedicine as possible

Ensure **process for reimbursement** in place (non-drug administrative costs)

Prepare for **reporting needs** for adverse events and record keeping

\(^2\) Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing.
Activity 1: Define facilities and patient visit logistics
Site will need dedicated outpatient COVID-19 treatment space

Dedicated COVID-19 patient area with needed infusion supplies

- Some sites using COVID-19 waiting rooms for monitoring post infusion
- Rededication of existing clinical space acceptable under CMS Hospital Without Walls Initiative

Immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the EMS, as necessary

Select recommendations for outpatient setting, for more information reference CDC guidelines
As part of CMS Hospital Without Walls initiative, hospitals can provide services outside of standard hospital settings

- **Other healthcare facilities** (e.g., urgent care clinics, doctors’ offices etc)
- **Remote locations or sites** not normally considered healthcare facilities, (e.g., patient home via telemedicine, hotels, community site, temporary tents)
- **Nursing home or home health services** also likely to be acceptable sites of administration

Alternate site of care will need **same core capabilities and supplies** as typical site of administration

- Facility and patient flow needs (page 15 and 17)
- Supplies needed on site (e.g., rescue medication, infusion supplies, etc – page 23)

Please reference CMS Hospitals Without Walls waivers and guidance for detailed information about program
Important to manage patient flow in a healthcare setting

- Have patient **wait to enter the site** until pre-scheduled time for treatment
- Ensure patient **wearing a mask or face covering** before entering the building
- Escort patient **directly to room, limit transport and movement of the patient outside of the room**
- Keep the **door closed** while patient in infusion room
- Medical and support personnel entering room need to **wear sufficient PPE** based on CDC guidelines
- Room should undergo **appropriate cleaning and surface disinfection** before it is returned to routine use

Select recommendations for outpatient setting, for more information reference CDC guidelines
Infusion preparation process:
- Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies
- Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter

Needs for space to prepare mAb drug:
- Dedicated preparation area with sufficient capacity onsite or nearby

Acceptable equipment for mAb drug storage:
- Functional pharmacy sink
- Refrigerated storage (2-8° C)
- Temperature monitoring system with back-up
- Alarm system for notification to authorized personnel of temperature deviations/excursions in place

Please see EUA manufacturer fact sheet for drug-specific requirements
Outpatient monoclonal antibody product likely to need administration early in symptom progression
  • Treatment should be administered as soon as possible following positive test result, and within 10 days of symptom onset

Fast turn-around testing capabilities key to identify patients and treat within this window
  • On-site point-of-care rapid testing or PCR tests ideal to provide quick diagnosis and treat patients on the same day
  • Alternatives include partnership with off-site testing facility nearby with reliable and quick turnaround and robust patient tracking and reporting mechanism
    - Accelerated testing results turnaround likely recommended to allow for infusion early in disease progression

Please reference EUA factsheet for detailed treatment guidelines including recommended treatment window
Distribution – Direct ordering for all three mAb products

- HHS/ASPR continues to manage the distribution of mAb products under EUA as stated in the FDA Letters of Authorization

- Given the current supply of product, bamlanivimab, casirivimab / imdevimab, and bamlanivimab / etesevimab can be requested via direct ordering for all sites (no further allocations to states are currently planned)

- Direct orders for casirivimab / imdevimab and bamlanivimab / etesevimab are limited to 48 patient courses per site/per week, though sites with higher utilization can request additional courses

- Questions regarding the direct order process: HHS: COVID19Therapeutics@hhs.gov ABC: C19therapies@amerisourcebergen.com

Information on direct order process available at phe.gov –

High level guidance on product shipping and storage

Product will be shipped refrigerated (2-8° C) to your location by USG distribution partners.

Product should be stored refrigerated (2-8° C) before use.

Target shelf-life for product ~10 months at minimum, follow guidance from manufacturer on expiration dates and product turnover.

Prepared IV solutions are intended for immediate patient administration. If not used immediately:

- Solutions may be held at refrigerated conditions for example:
  - Eli Lilly no more than 24 hours
  - Regeneron no more than 36 hours
- Solutions may be held at ambient light and room temperature conditions (including preparation, solution hold, infusion and flush) for example:
  - Eli Lilly no more than 7 hours
  - Regeneron no more than 5 hours

Please adhere to all guidelines for storage and use provided by manufacturer of EUA product.
Activity 2: Ensure sufficient supplies
Site supplies needed: Standard infusion supplies are needed but several components have been difficult to source

Sites interested in providing outpatient infusions of mAbs to COVID+ patients should:

1. Confirm sufficient supplies of infusion materials
2. Proactively ensure items with long-lead times are sourced for your site

Ensure supplies sufficient to cover mAbs treatment in addition to day-to-day operations needs

**List of suggested supplies (not exhaustive)**

**PPE**
- Gloves
- Gowns
- Eye and face protection (e.g. goggles, safety glasses, face shields)
- NIOSH-certified, disposable N95 filter facepiece respirators or better

**Infusion supplies**
- Infusion chairs – *recommended only*
- IV pole
- IV administration sets
  - PVC infusion set with/without DEHP containing 0.2 or 0.22 micron polyethersulfone (PES) in-line filter
- IV and catheters
- 3mL saline syringes
- Appropriately sized syringes
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Tegaderm bio-occlusive dressing
- Absorbent underpads (blue pads)
- Extension set tubing
- Needles – stainless steel 18ga
- Sharps containers
- Transpore tape
- Transilluminator (vein finder)

**General supplies**
- Infusion Reaction Kit
- Vital signs equipment
- Crash cart or Emergency Medical Management Equipment and Backboard
- Refrigerator
  - Optional to store prepared solution onsite
- Privacy screens
- Biohazard disposal bag
- Disposable disinfecting wipes
- Thermometer probe covers (if required)
- 70% alcohol wipes
- Paper towels
- Trash bins and liners

Please reference EUA factsheet for final requirements
Activity 3: Develop plan for staffing and personnel
Prescribe monoclonal antibody to patient, answer questions and respond in case of emergency
  
  - Infectious disease or general HCP
  - HCP will need to be on site or available telehealth or phone for treatment
  - At least 1 provider (nurse or HCP) onsite should be able to respond to medical emergency (e.g., severe infusion reaction); any specific certifications based on state and healthcare facility regulations and policies

Prepare the infusion, answer questions and support with monoclonal antibody storage
  
  - Pharmacy does not need to be physically located at the site of infusion
  - The infusion can be prepared by any qualified medical professional

Administer patient infusion (up to 1 hr) and monitor patient wellbeing (1 hr)
  
  - May require 2 nurses to start infusion, nurse practitioner to oversee larger infusion unit (if needed)
  - Experienced phlebotomist needed as often difficult to find vein in patients (often high BMI and dehydrated)

Please reference EUA factsheet for specific treatment guidelines
## Needed roles and responsibilities for site

<table>
<thead>
<tr>
<th>Role</th>
<th>Needed skills/profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient intake</td>
<td>Scheduling and administrative skills</td>
</tr>
<tr>
<td>Drug preparation</td>
<td>Pharmacist, pharmacy technician, or nurse or other HCP trained in IV preparation</td>
</tr>
<tr>
<td>Infusion: Start IV</td>
<td>Nurse or other alternate healthcare team member trained to begin an IV</td>
</tr>
<tr>
<td>Infusion: Administer infusion</td>
<td>Nurse or other alternate healthcare team member trained in administering an IV</td>
</tr>
<tr>
<td>Infusion monitoring</td>
<td>Nurse or other alternate healthcare team member trained in vital sign monitoring</td>
</tr>
<tr>
<td>Post infusion observation</td>
<td>Nurse or other alternate healthcare team member trained in vital sign monitoring</td>
</tr>
<tr>
<td>Patient release</td>
<td>Administrative skills, or nurse or other alternate healthcare team member as required</td>
</tr>
<tr>
<td>Cleaning</td>
<td>Person trained in COVID cleaning / disinfection</td>
</tr>
</tbody>
</table>
Activity 4: Review drug administration process
Three potential treatment pathways for symptomatic COVID-19 patients to receive care

Scenario 1: Patient tests positive and referred to site
- Treatment scheduled for infusion as soon as possible following result
- Patient counseled and assents to treatment (if not completed earlier in process), then treated via infusion
- Patient completes monitoring and leaves the facility, telemedicine follow-up

Scenario 2: Patient arrives for testing at site with unknown diagnosis
- Point-of-care testing performed, patient awaits results onsite
- Treatment scheduled for same day infusion
- Patient counseled and assents to treatment (if not completed earlier in process), then treated via infusion
- Patient completes monitoring and leaves the facility, telemedicine follow-up

Scenario 3: Patient arrives for testing at site with unknown diagnosis
- Patient tested, treatment discussed, sent home to await results
- If positive, proactive outreach to patients and treatment scheduled for infusion as soon as possible following result
- Treatment needed as soon as possible following positive test result and ≤10 days from onset of symptoms
- Please reference EUA factsheet for exact treatment window

Patient tested offsite, sent home to await results

Patient counselled

Patient completes monitoring and leaves the facility, telemedicine follow-up
## Patient flow for outpatient mAbs product

### Scenario 1: Confirmed positive patient referred for treatment

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
</table>
| **Confirm documentation of COVID-19 infection via either**  
  • Participant-provided lab report  
  • Medical record lab report  
  • Direct communication from a provider or laboratory | **Pre-book time for infusion space and follow clear protocol for coming onsite**  
  • Ensure operationally ready to receive and treat the patient  
  • Use CDC recommended practices to minimize exposure to others | **Discharge patient immediately following monitoring completion**  
  • Follow clear protocol to minimize risk of exposure to others |
| **Discuss treatment with patient**  
  • Ensure patient meets treatment requirements and understands risks | **Provide treatment to patient**  
  • Infusion duration up to ~1 hr with an additional 1 hr of observation post infusion (checks during infusion and observation)  
  • Infusion pumps or gravity-based infusion acceptable  
  • Ensure adequate staffing | **Post-treatment care encouraged to be via telemedicine as possible**  
  • Normal follow-up care, no special data tracking requirements |
| **Schedule the patient to come in for treatment ASAP**  
  • Provide guidance on site visit protocols to patients  
  • Provide patient education on what to expect with infusions |  |  |
| *Pre-treatment steps should be completed via telemedicine as possible (~30 mins)* |  |  |

3. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
Patient flow for outpatient mAbs product

**Scenario 2 and 3: Patient arrives for testing at site with unknown diagnosis**

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct patient to typical testing process for site (onsite or offsite)</strong></td>
<td>Pre-book time for infusion space and follow clear protocol for coming onsite</td>
<td>Discharge patient immediately following monitoring completion</td>
</tr>
<tr>
<td>- Quick response testing needed for early diagnosis to enable early treatment</td>
<td>- Ensure operationally ready to receive and treat the patient</td>
<td>- Follow clear protocol to minimize risk of exposure to others</td>
</tr>
<tr>
<td><strong>Assuming patient discharged to await test results, once patient confirmed positive outreach on treatment (~30 mins)</strong></td>
<td>- Use CDC recommended practices to minimize exposure to others</td>
<td><strong>Post-treatment care encouraged to be via telemedicine as possible</strong></td>
</tr>
<tr>
<td>- Discuss treatment with patient</td>
<td>- Provide treatment to patient</td>
<td>- Normal follow-up care, no special data tracking requirements</td>
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<td>- Provide guidance on infusions and site visit protocols to patients</td>
<td>- Infusion pumps or gravity-based infusion acceptable</td>
<td></td>
</tr>
<tr>
<td>- Schedule the patient to come in for treatment ASAP</td>
<td>- Ensure adequate staffing</td>
<td></td>
</tr>
<tr>
<td>- Pre-treatment discussion and scheduling should be via telemedicine as possible</td>
<td><strong>Ensure preparation for infusion reactions as unlikely but possible side effect</strong></td>
<td></td>
</tr>
<tr>
<td><strong>In case of point-of-care rapid testing, consider same-day infusions. Needs</strong></td>
<td>- Infusion rate may be reduced based on patient circumstances</td>
<td></td>
</tr>
<tr>
<td>- Isolated location for patient to wait</td>
<td>- Ensure emergency action plan in place; ability to activate EMS if necessary, a requirement for administration under EUA</td>
<td></td>
</tr>
<tr>
<td>- Availability of infusion space and staff</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. Contingent on product dilution, reference EUA fact sheet for dilution and infusion timing
# General Guidelines for Regeneron and Lilly mAbs

<table>
<thead>
<tr>
<th>Product</th>
<th>Eli Lilly Bamlanivimab</th>
<th>Eli Lilly Bamlanivimab &amp; Etesevimab</th>
<th>Regeneron Casirivimab (Regn 10933) &amp; Imdevimab (Regn 10987)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start</strong></td>
<td>• Begin with 50 mL, 100 mL, 150 mL, or 250 mL normal saline bag</td>
<td>• Begin with 50 mL, 100 mL, 150 mL, or 250 mL normal saline bag</td>
<td>• Begin with 250 ml normal saline bag</td>
</tr>
<tr>
<td><strong>Add</strong></td>
<td>• 20 ml bamlanivimab</td>
<td>• 20 mL bamlanivimab • 40 mL etesevimab</td>
<td>• 10 ml of casirivimab (Regn10933) • 10 ml of imdevimab (Regn 10987)</td>
</tr>
<tr>
<td><strong>Final Volume in IV Bag</strong></td>
<td>• 70 mL, 120 mL, 170 mL, or 270 mL</td>
<td>• 110 mL, 160 mL, 210 mL, or 310 mL</td>
<td>• 270 mL</td>
</tr>
</tbody>
</table>

**Notes for Regeneron:** CASIRIVIMAB AND IMDEVIMAB MUST BE ADMINISTERED TOGETHER AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY. Regeneron cocktail casirivimab & imdevimab are available in the following size vials: 2.5 ml vial 120 mg/ml AND 11.1 ml vial 120 mg/ml

**Notes for Eli Lilly:** BAMLANIVIMAB MAY BE ADMINISTERED AS COCKTAIL WITH ETESEVIMAB OR AS MONO THERAPY ALONE. ETESEVIMAB MUST BE ADMINISTERED TOGETHER WITH BAMLANIVIMAB AFTER DILUTION BY INTRAVENOUS (IV) INFUSION ONLY.
### Detailed product preparation guidelines for Regeneron and Lilly mAbs

<table>
<thead>
<tr>
<th>Product</th>
<th>Eli Lilly</th>
<th>Eli Lilly Combo</th>
<th>Regeneron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vials provided</td>
<td>• One - 20 mL vial of Bamlanivimab</td>
<td>• One - 20 mL vial of Bamlanivimab</td>
<td>• One - 11.1 mL vial Casirivimab (Regn10933)</td>
</tr>
<tr>
<td></td>
<td>• Two – 20 mL vial of Etesevimab</td>
<td>• Two – 20 mL vial of Etesevimab</td>
<td>• One - 11.1 mL vial Imdevimab (Regn10987)</td>
</tr>
<tr>
<td></td>
<td>• One - 11.1 mL vial Casirivimab (Regn10933)</td>
<td>• Four - 2.5 mL vials Casirivimab (Regn10933)</td>
<td>• Four - 2.5 mL vials Imdevimab (Regn10987)</td>
</tr>
<tr>
<td></td>
<td>• Four - 2.5 mL vials Casirivimab (Regn10933)</td>
<td>• One - 11.1 mL vial Imdevimab (Regn10987)</td>
<td>• One - 11.1 mL vial Imdevimab (Regn10987)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initial 0.9% saline bag required</th>
<th>• 50 mL, 100 mL, 150 mL, or 250 mL</th>
<th>• 50 mL, 100 mL, 150 mL, or 250 mL</th>
<th>• 250 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required saline to remove from bag</td>
<td>• N/A</td>
<td>• N/A</td>
<td>• N/A</td>
</tr>
<tr>
<td>Volume product to withdraw from vial(s) and dilute in bag</td>
<td>• 20 mL Bamlanivimab from 1x 20mL vial</td>
<td>• 20 mL Bamlanivimab from 1x 20mL vial</td>
<td>• 10 mL Casirivimab from 1x 11.1 mL vial</td>
</tr>
<tr>
<td></td>
<td>• 40 mL Etesevimab from 2x 20mL vial</td>
<td>• 10 mL Etesevimab from 2x 20mL vial</td>
<td>• 10 mL Imdevimab from 1x 11.1 mL vial</td>
</tr>
<tr>
<td></td>
<td>• 110 mL, 160 mL, 210 mL, or 310 mL</td>
<td>• 10 mL Imdevimab from 4x 2.5 mL vial</td>
<td>• 10 mL Imdevimab from 4x 2.5 mL vial</td>
</tr>
<tr>
<td></td>
<td>• 270 mL</td>
<td>• 10 mL Imdevimab from 4x 2.5 mL vial</td>
<td>• 10 mL Casirivimab from 4x 2.5 mL vial</td>
</tr>
<tr>
<td></td>
<td>• 270 mL</td>
<td>• 10 mL Imdevimab from 1x 11.1 mL vial</td>
<td>• 10 mL Casirivimab from 4x 2.5 mL vial</td>
</tr>
<tr>
<td>Final volume of product in IV bag</td>
<td>• 70 mL, 120 mL, 170 mL, or 270 mL</td>
<td>• 270 mL</td>
<td>• 270 mL</td>
</tr>
<tr>
<td></td>
<td>• 110 mL, 160 mL, 210 mL, or 310 mL</td>
<td>• 270 mL</td>
<td>• 270 mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>• 270 mL</th>
</tr>
</thead>
</table>
Dose packs for REGEN-COV casirivimab and imdevimab

New packaging presentation of casirivimab and imdevimab containing one treatment dose of REGEN-COV available beginning in February 2021

Each REGEN-COV Dose Pack is delivered in a plastic bag and contains:

- **Sufficient number of vials** of casirivimab (REGN10933) and imdevimab (REGN10987) to prepare one treatment dose – since both casirivimab and imdevimab are available in different sizes, REGEN-COV Dose Packs may contain **2, 5 or 8 vials**
- A **1-page Information Sheet**
- A sticker on bag with name REGEN-COV and the NDC based on the combination of cartons contained within the dose pack

In addition to REGEN-COV Dose Packs, single cartons of casirivimab and imdevimab will still be in distribution – see next page for examples.
## REGEN-COV Requires 10ml of Casirivimab AND 10 ml of Imdevimab

<table>
<thead>
<tr>
<th>Casirivimab</th>
<th>Imdevimab</th>
</tr>
</thead>
<tbody>
<tr>
<td>casirivimab (Regn10933) Use a single 11.1ml vial Only use 10ml Discard the remaining 1.1ml</td>
<td>imdevimab (Regn10987) Use a single 11.1 ml vial Only use 10ml Discard the remaining 1.1ml</td>
</tr>
<tr>
<td>casirivimab (Regn10933) Use a single 11.1ml vial Only use 10ml Discard the remaining 1.1ml</td>
<td>imdevimab (Regn10987) Use four 2.5 ml vials = 120mg/ml</td>
</tr>
<tr>
<td>casirivimab (Regn10933) Use four 2.5 ml vials = 10ml</td>
<td>imdevimab (Regn10987) Use a single 11.1 ml vial Only use 10ml Discard the remaining 1.1ml</td>
</tr>
<tr>
<td>casirivimab (Regn10933) Use four 2.5 ml vials = 10ml</td>
<td>imdevimab (Regn10987) Use four 2.5 ml vials = 10ml</td>
</tr>
</tbody>
</table>

**Note:** Variation in carton and labeling may be encountered – refer to playbook for other variations [https://www.regeneroneua.com/Content/pdf/treatment-covid19-eua-guide-book.pdf](https://www.regeneroneua.com/Content/pdf/treatment-covid19-eua-guide-book.pdf)
Activity 5: Prepare for reimbursement and ordering
Reimbursement process for mAbs therapeutic under EUA

**Connect with state or territory health authority** on appropriate ordering procedures to receive mAbs product

Under initial phase of treatment (likely through 2020), **drug cost likely to be paid by US government** under advanced purchase agreements

**Confirm internally with your site** administration on reimbursement for **non-drug costs** (e.g., infusion services, pharmacy)

Please **reference CMS resources** for more information

- **Provider toolkit:** https://www.cms.gov/covidvax
- **COVID FAQs:**
# CMS: Coverage of Monoclonal Antibody Products to Treat COVID-19

## Medicare

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Payable by Medicare</th>
<th>Expected Patient Cost-Sharing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Hospital</td>
<td>✔</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Hospital or &quot;Hospital without Walls&quot;</td>
<td>✔</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Physician Office/Infusion Center</td>
<td>✔</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Nursing Home (See third bullet in Key Facts on CMS enforcement discretion)</td>
<td>✔</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Home</td>
<td>✔</td>
<td>No patient cost-sharing</td>
</tr>
</tbody>
</table>

1. Services must be furnished within the scope of the product’s FDA authorization or approval and within the provider’s scope of practice.
2. Under the Hospital Without Walls initiative, hospitals can provide hospital services in other healthcare facilities and sites that would not otherwise be considered to be part of a healthcare facility, or can set up temporary expansion sites to help address the urgent need to increase capacity to care for patients.
3. Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn’t participate in Medicare.

### Expected Payment to Providers: Key Facts

- Medicare payment for monoclonal antibody products to treat COVID-19 is similar across sites of care, with some small differences.
- Medicare pays for the administration of monoclonal antibody products to treat COVID-19. For example, Medicare will pay a national average of approximately $310 for the administration of certain monoclonal antibody products.
- CMS will exercise enforcement discretion to allow Medicare-enrolled immunizers working within their scope of practice and subject to applicable state law to bill directly and receive direct reimbursement from the Medicare program for administering monoclonal antibody treatments to Medicare Part A Skilled Nursing Facility residents.
- Medicare will pay the provider for these monoclonal antibody products when they are purchased by the provider. Medicare won’t pay if the product is given to the provider for free by, for example, a government entity.
- When purchased by the provider, Medicare payment is typically at reasonable cost or at 95% of the Average Wholesale Price (an amount determined by the manufacturer). These payment amounts vary depending on which type of provider is supplying the product. Original Medicare will pay for these products for beneficiaries enrolled in Medicare Advantage.
- For more specific information about Medicare payments to providers for these monoclonal antibody products, please see these Frequently Asked Questions.

Eli Lilly product codes
Q0239:
• Long descriptor: Injection, bamlanivimab-xxxx, 700 mg
• Short descriptor: bamlanivimab-xxxx
M0239:
• Long Descriptor: intravenous infusion, bamlanivimab-xxxx, includes infusion and post administration monitoring
• Short Descriptor: bamlanivimab-xxxx infusion

Regeneron product codes
Q0243:
• Long descriptor: Injection, casirivimab and imdevimab, 2400 mg
• Short descriptor: casirivimab and imdevimab
M0243:
• Long Descriptor: intravenous infusion, casirivimab and imdevimab includes infusion and post administration monitoring
• Short Descriptor: casirivimab and imdevimab infusion

Activity 6: Reporting process
Sites receiving monoclonal antibody will follow established mechanisms for tracking and reporting **serious adverse events**

- Events that are potentially attributable to monoclonal antibody use must be reported to the FDA
  - Refer to the Fact Sheet for Healthcare Providers as part of EUA for guidance
  - Complete and submit a MedWatch form or complete and fax FDA Form 3500 to report

Site must **maintain records** regarding use of the monoclonal antibody by patients

- **Inventory information:** e.g., lot numbers, quantity, receiving site, receipt date, product storage
- **Patient information:** e.g., patient name, age, disease manifestation, number of doses administered per patient, other drugs administered

USG will track product delivery through the commercial distributor and CMS systems

Ensure that any records associated with this EUA are **maintained for inspection** upon request
Thank you!